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☐ 1: J Mol Biol 1998 Dec 11;284(4):1141-51

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The fibronectin type III domain as a scaffold for novel binding proteins.

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The fibronectin type III domain (FN3) is a small autonomous folding unit which occurs in many animal proteins involving in ligand binding. The beta-sandwich structure of FN3 closely resembles that of immunoglobulin domains. We have prepared a phage display library of FN3 in which residues in two surface loops were randomized. We have selected mutant FN3s which bind to a test ligand, ubiquitin, with significant affinities, while the wild-type FN3 shows no measurable affinity. A dominant clone was expressed as a soluble protein and its properties were investigated in detail. Heteronuclear NMR characterization revealed that the selected mutant protein retains the global fold of FN3. It also has a modest conformational stability despite mutations at 12 out of 94 residues. These results clearly show the potential of FN3 as a scaffold for engineering novel binding proteins. Copyright 1998 Academic Press.

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